WEST Search History

DATE: Wednesday, December 11, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L3	l1 and L2	6	L3
L2	vector same (P1 replicon and factor)	7	L2
L1	method near3 clon$	12229	L1

END OF SEARCH HISTORY

$%^STN;HighlightOn= ***;HighlightOff=*** ;

Welcome to STN International! Enter x:x

LOGINID:ssspta1633cxq

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

********** Welcome to STN International **********

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4 Apr 09 ZDB will be removed from STN
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 30 NETFIRST to be removed from STN
NEWS 16 Aug 08 CANCERLIT reload
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28 Oct 21 EVENTLINE has been reloaded
NEWS 29 Oct 24 BEILSTEIN adds new search fields
NEWS 30 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 32 Nov 18 DKILIT has been renamed APOLLIT
NEWS 33 Nov 25 More calculated properties added to REGISTRY
NEWS 34 Dec 02 TIBKAT will be removed from STN
NEWS 35 Dec 04 CSA files on STN

NEWS EXPRESS October 14 CURRENT WINDOWS VERSION IS V6.01,
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

********** STN Columbus **********

FILE 'HOME' ENTERED AT 12:04:34 ON 11 DEC 2002

=> FIL BIOSIS EMBASE CAPLUS
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'BIOSIS' ENTERED AT 12:04:41 ON 11 DEC 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 12:04:41 ON 11 DEC 2002
COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE 'CAPLUS' ENTERED AT 12:04:41 ON 11 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s vector (3s) (p1 replicon and factor)
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
Certain operators may not be nested in combination with other operators. A nested operator is valid only when it occurs at the same level or above the operator outside the nested phrase as determined by the following precedence list:

1. Numeric
2. (W), (NOTW), (A), (NOTA)
3. (S), (NOTS)
4. (P), (NOTP)
5. (L), (NOTL)
6. AND, NOT
7. OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L) is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> s p1 replicon and F factor
L1 1 P1 REPLICON AND F FACTOR

=> d bib abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 1999:90263 CAPLUS
DN 130:134980
TI Shuttle vectors containing replication origins and selection markers for both yeast and bacteria
IN Bradshaw, M. Suzanne; Bollekens, Jacques A.; Ruddle, Frank H.
PA Yale University, USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5866404	A	19990202	US 1996-761704	19961206
US 5972614	A	19991026	US 1997-987966	19971210
US 6221588	B1	20010424	US 1998-95372	19980610
US 2002132348	A1	20020919	US 2000-729043	20001204

PRAI US 1995-8250P P 19951206
US 1996-761704 A2 19961206
US 1996-32645P P 19961210
US 1998-95372 A1 19980610
AB Claimed is a yeast-bacteria shuttle vector comprising both yeast and bacterial replication origins and selection marker genes, where the bacterial replication origin is either from the ***P1*** ***replicon*** or the ***F*** ***factor*** origin of replication. The functional anal. of genes frequently requires the manipulation of large genomic regions. A yeast-bacteria shuttle vector is described, that can be used to clone large regions of DNA by homologous recombination. The important feature of present invention is the presence of the a bacterial replication origin, which allows large DNA insert capacity. The utility of this vector lies in its ability to isolate, manipulate and maintain large fragments in bacteria and yeast, allowing for mutagenesis by yeast genetics and simplified prepn. of plasmid DNA in bacteria.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s p1 and replicon
L2 250 P1 AND REPLICON

=> s p1 (3a) replicon
L3 78 P1 (3A) REPLICON

=> s F (3a) factor?
L4 10056 F (3A) FACTOR?

=> s l3 and l4
L5 3 L3 AND L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 2 DUP REM L5 (1 DUPLICATE REMOVED)

=> s l6 not l1
L7 1 L6 NOT L1

=> d bib abs

L7 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1984:298540 BIOSIS
DN BA78:35020
TI P-1 PLASMID REPLICATION REPLICON STRUCTURE.
AU ABELES A L; SNYDER K M; CHATTORAJ D K
CS LAB. MOL. BIOL., LBI-BASIC RES. PROGRAM, NCI-FREDERICK CANCER RES. FAC.,
P.O. BOX B, FREDERICK, MD 21701, USA.
SO J MOL BIOL, (1984) 173 (3), 307-324.
CODEN: JMOBAK. ISSN: 0022-2836.
FS BA; OLD
LA English
AB Phage P1 lysogenizes Escherichia coli as a unit-copy plasmid. The plasmid-encoded elements implicated on P1 plasmid maintenance were defined. A 2081 base-pair fragment of the 90,000 base P1 plasmid confers the capacity for controlled plasmid replication. DNA sequence analysis reveals several open reading frames in this fragment. The largest is shown to encode a 32,000 MW protein required for plasmid replication. The corresponding gene, repA, was identified genetically. A set of five 19 base-pair repeats is located upstream from repA; a set of 9 similar repeats is located immediately downstream from repA. Each set of repeats, when cloned into pBR322, exerts incompatibility towards a ***P1*** ***replicon*** . The upstream set, designated incC, consists of direct repeats that are spaced about 2 turns of the DNA helix apart; the downstream set, designated incA, consists of 9 repeats arranged 3 in one orientation and 6 in the other. Spacing between incA repeats were 3 or 4 turns of the helix apart. The organization of the plasmid maintenance regions of P1 and the unit-copy sex ***factor*** plasmid, ***F*** , is strikingly similar. Although the DNA sequences of this region in the 2 plasmids exhibit little homology, a 9 base-pair sequence that appears 4 times in the origin region of members of the Enterobacteriaceae also occurs twice as direct repeats in similar positions in P1 and F. This sequence, where it occurs in E. coli, was postulated to be the binding site for the essential replication protein determined by dnaA. The dnaA protein appears not to be essential for the replication of either plasmid; the function of the sequence in P1 and F may be regulatory.

=> s knock in or knock-out
L8 11698 KNOCK IN OR KNOCK-OUT

=> d his

(FILE 'HOME' ENTERED AT 12:04:34 ON 11 DEC 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 12:04:41 ON 11 DEC 2002
L1 1 S P1 REPLICON AND F FACTOR
L2 250 S P1 AND REPLICON
L3 78 S P1 (3A) REPLICON
L4 10056 S F (3A) FACTOR?
L5 3 S L3 AND L4
L6 2 DUP REM L5 (1 DUPLICATE REMOVED)
L7 1 S L6 NOT L1
L8 11698 S KNOCK IN OR KNOCK-OUT

=> s l3 and l8
L9 0 L3 AND L8

=> s homologo? recombin? (3s) yeast
L10 1498 HOMOLOGO? RECOMBIN? (3S) YEAST

=> s l10 and l8
L11 14 L10 AND L8

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12 8 DUP REM L11 (6 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L12 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2002:794235 CAPLUS
DN 137:274176
TI Homologous recombination in mismatch repair inactivated eukaryotic cells
IN Te Riele, Henricus Petrus Joseph; De Wind, Niels; Dekker-Vlaar, Helena Maria Johanna
PA Neth.
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Ser. No. 147,712, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002151059	A1	20021017	US 2001-884877	20010620
WO 9705268	A1	19970213	WO 1995-EP2980	19950726

W: AU, BR, CA, CN, JP, KR, MX, NO, NZ, RU, SE, SG, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
PRAI WO 1995-EP2980 W 19950726
US 1999-147712 B2 19990223
AB A mammalian cell having a mismatch repair-deficient phenotype is provided, where one or both alleles of a gene essential for mismatch repair, such as an Msh gene, are inactivated. Using this cell in a gene ***knock*** - ***out*** methodol. advantageously allows efficient homologous recombination, even when the DNA sequences of the donor and recipient sequences diverge by significantly more than 0.6%. The present invention relates to a method for modifying the genome of eukaryotic cells by homologous recombination using DNA sequences which substantially differ from the target locus with respect to the nucleotide sequence (0.1 to 30 % divergence) in the region where recombination takes place. Homologous recombination between diverged sequences is achieved by genetic or transitory inactivation of the cell's mismatch repair system.

L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:904488 CAPLUS
DN 136:51264
TI Altering eIF-2.alpha. translation activity in plants in response to environmental stress
IN Roth, Donald A.
PA University of Wyoming, USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001094558	A1	20011213	WO 2001-US18342	20010606

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-587789 A 20000606
AB The present invention relates to compns. and methods useful to alter translation of the eukaryotic initiation factor-2.alpha. (eIF-2.alpha.) in response to biotic and abiotic stress, or growth pattern adjustment in plants. Stress factors can include pathogen attack, wounding, drought, hypoxia, light, or temp. Furthermore, a ***knock*** - ***out*** construct of the eIF-2.alpha. gene is provided, capable of ***homologous*** ***recombination*** with the wild-type gene. Wheat eIF-2.alpha. was shown to be able to substitute for the ***yeast*** eIF2.alpha. in ***yeast*** SUI2 mutants. Similarly, it was shown to be functional in mammalian cells where it was phosphorylated by PKR kinase.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2001:245966 BIOSIS
DN PREV200100245966
TI Efficient rejoining of radiation-induced DNA double-strand breaks in vertebrate cells deficient in genes of the RAD52 epistasis group.
AU Wang, Huichen; Zeng, Zhao-Chong; Bui, Tu-Anh; Sonoda, Eiichiro; Takata, Minoru; Takeda, Shunichi; Iliakis, George (1)
CS (1) Department of Radiation Oncology of Kimmel Cancer Center, Jefferson Medical College, Thompson Building Room B-1, Philadelphia, PA, 19107 USA
SO Oncogene, (26 April, 2001) Vol. 20, No. 18, pp. 2212-2224. print.
ISSN: 0950-9232.
DT Article
LA English
SL English
AB Rejoining of ionizing radiation (IR) induced DNA DSBs usually follows biphasic kinetics with a fast (t50: 5-30 min) component attributed to DNA-PK-dependent non-homologous endjoining (NHEJ) and a slow (t50: 1-20 h), as of yet uncharacterized, component. To examine whether ***homologous*** ***recombination*** (HR) contributes to DNA DSB rejoining, a systematic genetic study was undertaken using the hyper-recombinogenic DT40 chicken cell line and a series of mutants defective in HR. We show that DT40 cells rejoin IR-induced DNA DSBs with half times of 13 min and 4.5 h and contributions by the fast (78%) and the slow (22%) components similar to those of other vertebrate cells with 1000-fold lower levels of HR. We also show that deletion of RAD51B, RAD52 and RAD54 leaves unchanged the rejoining half times and the contribution of the slow component, as does also a conditional ***knock*** ***out*** mutant of RAD51. A significant reduction (to 37%) in the contribution of the fast component is observed in Ku70-/- DT40 cells, but the slow component, operating with a half time of 18.4 h, is still able to rejoin the majority (63%) of DSBs. A double mutant Ku70-/-/RAD54-/- shows similar half times to Ku70-/- cells. Thus, variations in HR by several orders of magnitude leave unchanged the kinetics of rejoining of DNA DSBs, and fail to modify the contribution of the slow component in a way compatible with a dependence on HR. We propose that, in contrast to ***yeast*** , cells of vertebrates are 'hard-wired' in the utilization of NHEJ as the main pathway for rejoining of IR-induced DNA DSBs and speculate that the contribution of ***homologous***

recombination repair (HRR) is at a stage after the initial rejoining.

L12 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:190845 BIOSIS
DN PREV200000190845
TI Bryophytes as model systems.
AU Wood, Andrew J. (1); Oliver, Melvin J.; Cove, David J.
CS (1) Department of Plant Biology, Southern Illinois University-Carbondale, Carbondale, IL, 62901-6509 USA
SO Bryologist, (Spring, 2000) Vol. 103, No. 1, pp. 128-133.
ISSN: 0007-2745.
DT Article
LA English
SL English
AB Bryophytes have been powerful experimental tools for the elucidation of complex biological processes. Analysis of organisms from these ancient clades is an active and ongoing enterprise that will provide greater insight into the development, physiology, phylogenetics, and stress-induced cellular responses of plants. To maintain their relevance as experimental models, the analysis of mosses must expand to include modern molecular tools such as a knowledge of the genome via large-scale DNA sequencing, the ability to create transgenic individuals via transformation, and the capability to create gene ***knock*** -outs by ***homologous*** ***recombination*** . The availability of these molecular tools is limited when compared to flowering plants. However, in mosses such as Physcomitrella patens, Funaria hygrometrica, Ceratodon purpureus, and Tortula ruralis these tools are rapidly being developed for the study of molecular genetics. Efficient targeted gene disruption (i.e., ***homologous*** ***recombination***) is a well-established tool in both ***yeast*** and murine cells that until recently was unknown in any plant model system. Recently, Schaefer and Zryd (1997) demonstrated that efficient ***homologous*** ***recombination*** occurs in P. patens. The ability to perform efficient ***homologous*** ***recombination*** in P. patens is at present unique amongst all plants and represents an extremely powerful technique for the functional analysis of plant genes.

L12 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1998:165336 BIOSIS
DN PREV199800165336
TI I-SceI-induced gene replacement at a natural locus in embryonic stem cells.
AU Cohen-Tannoudji, Michel; Robine, Sylvie; Choulika, Andre; Pinto, Daniel; El Marjou, Fatima; Babinet, Charles; Louvard, Daniel; Jaisser, Frederic (1)
CS (1) INSERM U246, Faculte de Medecine X. Bichat, 16 rue H. Huchard, 75018 Paris France
SO Molecular and Cellular Biology, (March, 1998) Vol. 18, No. 3, pp. 1444-1448.
ISSN: 0270-7306.
DT Article
LA English
AB Gene targeting is a very powerful tool for studying mammalian development and physiology and for creating models of human diseases. In many instances, however, it is desirable to study different modifications of a target gene, but this is limited by the generally low frequency of ***homologous*** ***recombination*** in mammalian cells. We have developed a novel gene-targeting strategy in mouse embryonic stem cells that is based on the induction of endogenous gap repair processes at a defined location within the genome by induction of a double-strand break (DSB) in the gene to be mutated. This strategy was used to ***knock*** in an NH2-ezrin mutant in the villin gene, which encodes an actin-binding protein expressed in the brush border of the intestine and the kidney. To induce the DSB, an I-SceI ***yeast*** meganuclease restriction site was first introduced by gene targeting to the villin gene, followed by transient expression of I-SceI. The repair of the ensuing DSB was achieved with high efficiency (6 X 10-6) by a repair shuttle vector sharing only a 2.8-kb region of homology with the villin gene and no negative selection marker. Compared to conventional gene-targeting experiments at the villin locus, this represents a 100-fold stimulation of gene-targeting frequency, notwithstanding a much lower length of homology. This strategy will be very helpful in facilitating the targeted introduction of several types of mutations within a gene of interest.

L12 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1997:345271 BIOSIS
DN PREV199799644474
TI Efficient gene targeting in the moss Physcomitrella patens.
AU Schaefer, Didier G. (1); Zyrd, Jean-Pierre
CS (1) Laboratoire de Phytogenetique Cellulaire, Universite de Lausanne, Batiment de Biologie, CH-1015 Lausanne-Dorigny Switzerland
SO Plant Journal, (1997) Vol. 11, No. 6, pp. 1195-1206.
ISSN: 0960-7412.
DT Article
LA English
AB The moss Physcomitrella patens is used as a genetic model system to study plant development, taking advantage of the fact that the haploid gametophyte dominates in its life cycle. Transformation experiments designed to target three single-copy genomic loci were performed to determine the efficiency of gene targeting in this plant. Mean transformation rates were 10-fold higher with the targeting vectors and molecular evidence for the integration of exogenous DNA into each targeted locus by ***homologous*** ***recombination*** is provided. The efficiency of gene targeting determined in these experiments is above 90%, which is in the range of that observed in ***yeast*** and several orders of magnitude higher than previous reports of gene targeting in plants. Thus, gene ***knock*** - ***out*** and allele replacement approaches are directly accessible to study plant development in the moss Physcomitrella patens. Moreover, efficient gene targeting has so far only been observed in lower eukaryotes such as protozoa, yeasts and filamentous fungi, and, as shown here the first example from the plant kingdom is a haplobiontic moss. This suggests a possible correlation between efficient gene targeting and haplophase in eukaryotes.

L12 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 1997:391337 BIOSIS
DN PREV199799690540
TI Transposon-generated ' ***knock*** - ***out*** ' and ' ***knock*** -in' gene-targeting constructs for use in mice.
AU Westphal, Christoph Heiner (1); Leder, Philip
CS (1) Dep. Genetics, Harv. Med. Sch., 200 Longwood Ave., Boston, MA 02115 USA
SO Current Biology, (1997) Vol. 7, No. 7, pp. 530-533.
ISSN: 0960-9822.
DT Article
LA English
AB The conventional technique for targeted mutation of mouse genes entails placing a genomic DNA fragment containing the gene of interest into a vector for fine mapping, followed by cloning of two genomic arms around a selectable neomycin-resistance cassette in a vector containing thymidine kinase (1); this generally requires 1-2 months of work for each construct. The single ' ***knock*** - ***out*** ' construct is then transfected into mouse embryonic stem (ES) cells, which are subsequently subjected to positive selection (using G418 to select for neomycin-resistance) and negative selection (using FIAU to exclude cells lacking thymidine kinase), allowing the selection of cells which have undergone ***homologous*** ***recombination*** with the knockout vector. This approach leads to inactivation of the gene of interest (2). Recently, an in vitro reaction was developed, on the basis of the ***yeast*** Ty transposon, as a useful technique in shotgun sequencing (3). An artificial transposable element, integrase enzyme and the target plasmid are incubated together to engender transposition. The DNA is then purified, and subsequently electroporated into bacteria. The transposon and the target plasmid bear distinct antibiotic resistance markers (trimethoprim and ampicillin, respectively), allowing double selection for transposition events. In the present study, we have modified this system to allow the rapid, simultaneous generation of a palette of potential gene targeting constructs. Our approach led from genomic clone to completed construct ready for transfection in a matter of days. The results presented here indicate that this technique should also be applicable to the generation of gene fusion constructs (4-8), simplifying this technically demanding method.

L12 ANSWER 8 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 97000851 EMBASE
DN 1997000851
TI Recombinant DNA technology as an investigative tool in drug metabolism research.
AU Friedberg T.; Wolf C.R.
CS T. Friedberg, Biomedical Research Centre, Ninewells Hospital/Medical School, Dundee DD1 9SY, United Kingdom
SO Advanced Drug Delivery Reviews, (1996) 22/1-2 (187-213).
ISSN: 0169-409X CODEN: ADDREP
PUI S 0169-409X(96)00419-X
CY Netherlands
DT Journal; General Review
FS 022 Human Genetics
029 Clinical Biochemistry
036 Health Policy, Economics and Management
052 Toxicology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Drug metabolism influences the pharmaco-toxicological properties of a vast array of compounds and is controlled by a complex system of drug metabolizing enzymes. A thorough understanding of this system allows the more effective development of therapeutic drugs, as well as a significant improvement of risk assessment, particularly in the field of chemical carcinogenesis. The early identification of potential therapeutic problems relating to drug metabolism could reduce the development costs for pharmaceuticals. Recently, techniques using recombinant DNA have become available for this purpose. In these approaches the genetic information for the enzyme under investigation is expressed in vitro or in vivo, following gene transfer. This approach is called heterologous expression. In addition it is possible to inactivate genes in cells and animals by ***homologous*** ***recombination*** (gene-targeting, - ***knock*** ***out***). Heterologous expression and gene ***knock*** outs can be used to define the catalytic parameters as well as the biological role of xenobiotic metabolizing enzymes. Some heterologous expression systems supply sufficient amounts of these enzymes for structure/function

analysis, thus immensely improving the prospects of rational drug design. In addition, these systems provide the basis for rapidly generating immunological tools for the selective quantitation of xenobiotic metabolizing enzymes in human tissues. This combined with the knowledge about the catalytic parameters of a particular enzyme, allows predictions on the exact role of enzymes in drug metabolism as well as drug-drug interactions to be made. However in this regard an important and unfortunately often neglected issue is the appropriate validation of the different heterologous expression systems. Transgenes have also been used to study the regulation of drug metabolizing enzymes by endogenous and exogenous substances using reporter constructs. These studies may also lead to a thorough understanding of the mechanisms underlying interindividual differences in the level of xenobiotic metabolizing enzymes. This article surveys and critically examines the applicability of the different mammalian, ***yeast*** , insect and bacterial systems for evaluating the structure, the enzymatic function, the biological role and the regulation of drug metabolizing enzymes in vitro and in vivo.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		56.55	56.76

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	ENTRY	SINCE FILE SESSION	TOTAL
CA SUBSCRIBER PRICE		-1.86	-1.86

STN INTERNATIONAL LOGOFF AT 12:11:44 ON 11 DEC 2002